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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/047,253	01/14/2002	Gregory Cope	CIT1510-4	6270

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/047,253	COPE ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32,33,36,37,41-57,74,75 and 77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-33, 36-37, 41-57, 74-75 and 77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on April 7, 2005, amending claim 32-33, 47-48 and 74, canceling claims 34-35, 39, 72 and 73 and adding claim 77, has been entered.

Claims 32-33, 36-37, 41-57, 74-75 and 77 are pending and are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on April 7, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-33, 36-37, 41-57, 74-75 and 77 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of identifying agents that affects isopeptidase activity of a Rpn11, or Rpn11 complex or AMSH, wherein Rpn11, or Rpn11 complex or AMSH comprises a JAMM domain consisting of SEQ ID NO:1 and cleaves a modifier protein from a target protein. Therefore, these claims are drawn to a method of using a genus of polypeptides having any structure, including recombinants, variants and fragments of any or all Rpn11, or Rpn11 complex or AMSH. The specification only teaches a few representative species, Examples 1-3. These species are not enough to describe the whole genus of Rpn11, or Rpn11 complex or AMSH that cleaves any or all modifier protein from any or all target proteins. Even though the claims do limit the structure of the isopeptidase to a Rpn11, or Rpn11 complex or AMSH comprising the JAMM domains, the domain is insufficient in describing the structure of such a wide genus of Rpn11, or Rpn11 complex or AMSH that includes recombinants, variants or mutants of any or all Rpn11, or Rpn11 complex or AMSH. Rpn11, or Rpn11 complex or AMSH comprising only the JAMM domain of SEQ ID NOs: 1 or 2, of which only three residues are identified, may or may not cleave any modifier protein from a target protein. Therefore, these claims are drawn to a method of using a genus of polypeptides having any structure.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 32-33, 36-37, 41-57, 74-75 and 77.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov <http://www.uspto.gov>.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the claims have been amended to recite Rpn11, or RPN11 complex or AMSH" therefore, the claims are drawn to polypeptides having any structure. Examiner respectfully disagrees. While applicants have amended the claims to recite that the isopeptidase is Rpn11, or RPN11 complex or AMSH, the claims are drawn to any Rpn11, or RPN11 complex or AMSH that cleaves any or all modifier proteins and any or all target proteins. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.**

Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only a few species within the genus.

In the instant case, the specification describes a method of using a few specific Rpn11 and AMSH that cleaves specific modifier and target proteins, as described in Examples 1-3. However, the claimed genus comprise species which are widely variant in structure, wherein any Rpn11, or RPN11 complex or AMSH or variants must cleave any modifier proteins or any target proteins or variants thereof. As such, the description of only being a Rpn11, or RPN11 complex or AMSH, is insufficient to be representative of the attributes and features of the entire genus.

Hence the rejection is maintained.

Claims 32-33, 36-37, 41-57, 74-75 and 77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of using the Rpn11 and AMSH described in Examples 1-3 in the specification, does not reasonably provide enablement for a method of using any Rpn11, or Rpn11 complex or AMSH having any structure. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method of identifying agents that affects isopeptidase activity of a Rpn11, or Rpn11 complex or AMSH, wherein Rpn11, or Rpn11 complex or AMSH comprises a JAMM domain consisting of SEQ ID NO:1 and cleaves a modifier protein from a target protein. Therefore, these claims are drawn to a method of using a genus of polypeptides having any structure, including recombinants, variants and fragments of any or all Rpn11, or Rpn11 complex or AMSH. Therefore, the breadth of these claims is much larger than the scope enable by the specification.

Even though the claims do limit the structure of the polypeptide to a Rpn11, or Rpn11 complex or AMSH the JAMM domain of SEQ ID NO:1, the claims encompass a method of using any or all Rpn11, or Rpn11 complex or AMSH that cleaves any or all modifier proteins and any or all target proteins. Not all Rpn11, or Rpn11 complex or AMSH comprising the JAMM domain of SEQ ID NO: 1 may cleave any or all modifier proteins and any or all target proteins. The specification only teaches a method using

Rpn11 and AMSH that cleaves specific modifier and target proteins, as described in Examples 1-3. The quantity of experimentation in this area is extremely large and it would require significant study to identify any or all Rpn11, or Rpn11 complex or AMSH that cleaves any or all modifier proteins and any or all target proteins and would be an inventive, unpredictable and difficult undertaking. This would require years of inventive effort, with each of the many intervening steps, upon effective

While recombinant techniques are available, it is not routine in the art to screen large numbers of amino acids where the expectation of obtaining similar sequences is unpredictable. The amino acid sequence determines the structural and functional properties of an enzyme.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a method of using any or all Rpn11, or Rpn11 complex or AMSH that cleaves any or all modifier proteins and any or all target proteins. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the isopeptidase having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that all 8 factors of *In re Wands* have been satisfied. Examiner respectfully disagrees. While applicants have amended the claims to recite that the isopeptidase is Rpn11, or RPN11 complex or AMSH, the claims are drawn to any Rpn11, or RPN11 complex or AMSH, including variants, recombinants, or mutants, that cleaves any or all modifier proteins and any or all target proteins. In order to practice the claimed method, one of ordinary skill in the art must make or select all the encompassed Rpn11, or RPN11 complex or AMSH that cleaves any or all target and modifier proteins. However, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a specific knowledge of and guidance with regard to which specific amino acids in the protein's sequence, can be modified such that the modified polypeptide continues to have said claimed activity, or in the instant application ability of the Rpn11, or RPN11 complex or AMSH to cleave any modifier and target protein. It is this specific guidance that applicants do not provide. Without specific guidance, those skilled in the art will be subjected to undue experimentation of making and testing each of the enormously large number of Rpn11, or RPN11 complex or AMSH that results from such experimentation. The claims require an undue experimentation one of ordinary skill in the art to practice the claimed method.

Hence the rejection is maintained.

None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

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